## REMARKS/ARGUMENTS:

Reconsideration of the above identified application is respectfully requested.

In the Office action dated May 11, 2004, claims 4, and 5 are rejected under 35 U.S.C. §102(b) as being anticipated by Dorson et al. (Journal of Fish Diseases, 1978, 1:309-320; hereinafter "Dorson"). Claims 1, 3-5, 8, 10-14, 17 and 18 are rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,274,147 to Vakharia et al. (hereinafter "Vakharia"). The Examiner is thanked for pointing out claims 6, 7, 15 and 16 are free of prior art of record.

Applicants also acknowledge safe receipt of the "Notice of References Cited" (form PTO-892) and cited reference.

In response to the rejections, Applicant has decided to amend claim 1 to incorporate the limitations of claim 6 into the amended claim 1. Also, Applicant has converted claim 8 into an independent claim and further incorporated the limiation of claim 15 into the amended claim 8. As a result, claims 6 and 15 are cancelled. Furthermore, claims 1 and 8 are further amended to change the phrase "is produced in" to -- is obtained from -- to further clarify the invention. Since the Examiner has indicated that claims 6-7, and 15-16 are patentable, the amended claims 1 and 8, which contain the limitations of claims 6 and 15, should be allowable. In addition, claims 3, 7, 10, and 16, which are depending upon the amended claims 1 and 8, respectively, should also be allowable.

In addition, Applicant has amended claims 4 and 11 to incorporate the limitation of claim 13 into claims 4 and 11. As a result, claim 13 is cancelled. In addition, claims 4 and 11 are further amended to change the phrase "is produced in" to -- is obtained from -- to further clarify the invention. Claim 14 is amended to correct the dependency of the claim from claim 13 to claim 11 because claim 13 has been cancelled. Claim 17 is cancelled. Due to the cancellation of

claim 17, claim 18 is amended to change the dependency of the claim from claim 17 to claim 4. These amendments are conform to the practice after final. No new matter has been introduced.

In addition to the cancellation and amendments of the claims, a 132 declaration is submitted accompanying this response in support of Applicant's claim that the claimed invention is unobviously different from that of the prior art product, because the GF-1 cell line, which is derived from grouper, is not supposed to be a susceptible host for IPNV, but, as the comparative studies shown, IPNV in fact is propagated in the GF-1 cell line far better than that in the CHSE-214 cell line (a salmon cell line), which is known to be susceptible to IPNV.

Applicants respectfully submit that the amendments of claims 4 and 11 have overcome the rejections under 35 U.S.C. §§ 102(b) and (e) for the reasons set forth below.

### *Claim Rejections Under 35 U.S.C. § 102(b)*

Claims 4 and 5 are rejected under 35 U.S.C. § 102(b) as being anticipated by Dorson et al. (Journal of Fish Diseases 1978, 1:309-320). The Examiner alleges that "Dorson et al. clearly teach an immunologically effective amount of an infectious pancreatic necrosis virus (IPNV) vaccine for immunizing trout. *See* Office Action at 2. Specifically, the Examiner alleges that due to Applicant's recitation of the phrase "wherein said IPNV is produced in an immortal cell line...", the claim is a product-by-process claim. The Examiner further asserts that "where a product-by-process claim is rejected over a prior art product that appears to be identical, although produced by a different process, the burden is upon the applicants to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product." *See* Office Action at 3.

Applicant disagrees with the Examiner's characterization of claims 4-5 as product-by-process claim. In order to clarify that claims 4 and 5 are not product-by-process claims, Applicant has amended the phrase "is produced in" to -- is obtained from -- to ensure that the claim is not to be construed as product-by-process claim. In addition, a 132 declaration is submitted, in which the declarer presented her comparative studies regarding the IPNV propagation between the GF-1 and the CHSE-214 cell line. The GF-1 cell line derives from *Epinephelus coioides* (grouper), which is known not a susceptible host for IPNV (meaning that IPNV would not be able to propagate in grouper). CHSE-214 cell line, on the other hand, is a cell line derived from Chinook salmon embryonic cells, which is known to be susceptible to IPNV. However, the results of the comparative studies show, contrary to the conventional belief, IPNV not only propagates well in the GF-1 cell line, but propagates in a titer of almost twice of that in the CHSE-214 cells. This clearly constitutes an unexpected result which should no doubt support Applicant's claim that the IPNV obtained from GF-1 cell line is different from the IPNV obtained from RTG-2 cells as disclosed in Dorson et al. RTG-2 cells are cells derived from Rainbow trout gonad which is known to be susceptible to IPNV (*i.e.*, Rainbow trout belongs to the salmonid species).

In addition, Dorson et al. never discloses the use of an inactivated IPNV for vaccine.

To anticipate a claim, each and every element of the claim must be taught, either expressly or inherently, in a single prior art reference. *See e.g., Verdegaal Bros. v. union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) ("a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference").

Since Dorson et al. do not teach the claim limitation that "IPNV is an inactivated virus," claims 4-5 are not anticipated by Dorson et al.

***Claim Rejection Under 35 U.S.C. § 102(e)***

Claims 1, 3-5, 8 and 10-14, 17-18 are rejected under 35 U.S.C. § 102(e) as being anticipated by Vakharia et al., U.S. Pat. No. 6,274,147 B1 ("Vakharia et al."). Specifically, the Examiner alleges that "Vakharia et al. teach both live, non-pathogenic infectious pancreatic necrosis virus (IPNV) vaccines and inactivated IPNV vaccines. Nodavirus (which comprise various NNV species) chimeric vaccines are also taught." *See* Office Action at 4.

With regard to claim 1, Applicant has amended the claim to incorporate the limitation of claim 6, *i.e.*, "the IPNV is an inactivated virus." Since the Examiner indicates that claim 6 is allowable, the amended claim 1 and its dependant claims 3, 8, and 10, should now be allowable.

With regard to claims 4-5, 11-14, and 17-18, Applicant has amended claims 4 and 11 to change the phrase "is produced in" to -- is obtained from -- to ensure that it is now clear that the claims are not "product-by-process" claims. Also, as set forth in Applicant's arguments traversing the 102(b) rejections and the attached 132 declaration, *supra*, which is incorporated by reference, the IPNV obtained from the GF-1 cell line is unobviously distinctively different from the IPNV from CHSE cells taught in Vakharia et al., or any IPNV derived from a susceptible host of IPNV.

Since Vakharia et al. do not teach the limitation that the IPNV is obtained from the GF-1 cell line, Applicant's claimed invention is not anticipated by Vakharia et al.

In view of the foregoing, the objection and rejections have been overcome and the claims are in condition for allowance, early notice of which is requested. Should the application not be passed for issuance, the examiner is requested to contact the applicant's attorney to resolve the problem.

Respectfully submitted,

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Date: September 2, 2005

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| Serial No.: | **10/004,432** | | |
| Applicants: | **Shau-Chi CHI** | TC/A.U.: | **1648** |
| Filed: | **December 6, 2001** | Examiner: | **Laurie A Scheiner** |
| Title: | **AN IMMORTAL CELL LINE DERIVED FROM GROUPER *EPINEPHELUS COIOIDES* AND ITS APPLICATIONS THEREIN** | **Customer No.:** | *23639* PATENT TRADEMARK OFFICE |
| Docket No.: | **SC7040694001 (formerly 39734-176754)** | | |

**DECLARATION OF DR. KJERSTI GRAVINGEN PURSUANT TO 37 C.F.R. § 1.132**

I, Dr. Kjersti Gravingen, hereby declare:

1. I am a researcher in the field of fish diseases and vaccine development. I am currently employed by Pharmaq AS in Norway. Pharmaq AS is the exclusive licensee of the GF-1 cell line having an ATCC deposit No. of PTA-859. Pharmaq AS is located in Skøyen, N-0213, Oslo, Norway.

2. In connection with my research in developing vaccines for immunizing susceptible fish against infection by Infectious Pancreatic Necrosis Virus (IPNV), I have studied the propagation of IPNV in the GF-1 and CHSE-214 cell lines. CHSE-214 cell line is an immortal fish cell line derived from Chinook salmon embryonic cells.

3. The "Materials and Methods" I used are summarized as follows:

*(A) Materials:*

(i) The CHSE-214 cell line is grown in a growth medium containing EMEM (Sigma M7278, FBS (Sigma); L-glutamin (Sigma G7513); and Gentamicin (Sigma G1397).

(ii) The GF-1 cell line is grown in a growth medium containing L-15 (Sigma L5520); FBS (Sigma); L-glutamin (Sigma G7513); and Gentamicin(Sigma G1397).

***(b) Methods***

The GF-1 and CHSE-214 cell lines were cultivated and passed 3 times on the growth medium containing serum before seeding of 13 cell culture flasks with each cell line. The GF-1 cells were seeded with a density of $3 \times 10^4$ C/cm$^2$ and CHSE with a density of $4 \times 10^4$ C/cm$^2$. Two flasks from each of the four groups were trypsinated and counted 3, 4, 5, 6 and 7 days after seeding. The cell counts 7 days after cell seeding were used to calculate the virus input for the remaining three flasks within each group. The infection was performed by replacing of the growth medium with fresh medium containing 2% of FBS and IPNV corresponding to a MOI of 0.1. The CHSE-214 and GF-1 flasks were incubated 3 and 5 days at 15$^0$C before sampling, respectively. The titration was performed on plates prepared from CHSE-214 cell cultures with serum. Samples from CHSE-214 cells were titrated on fresh material, whereas the GF-1 samples were frozen before titration.

4. The results of my studies are summarized as follows:

***(A) Cell growth promotion test***

The average doubling time for the CHSE-214 cells were 2.2 days (figure 1). The average doubling time for the GF-1 cells were 1.2 days (figure 2).

**Figure 1.** Cell growth promotion test on CHSE-214 cells with Sigma serum in 75 $cm^2$ cell culture flasks. Two flasks were counted at each time point.

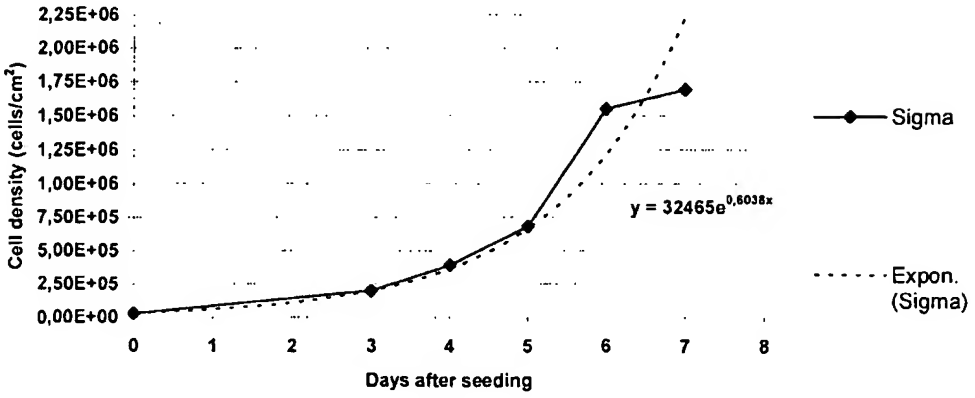
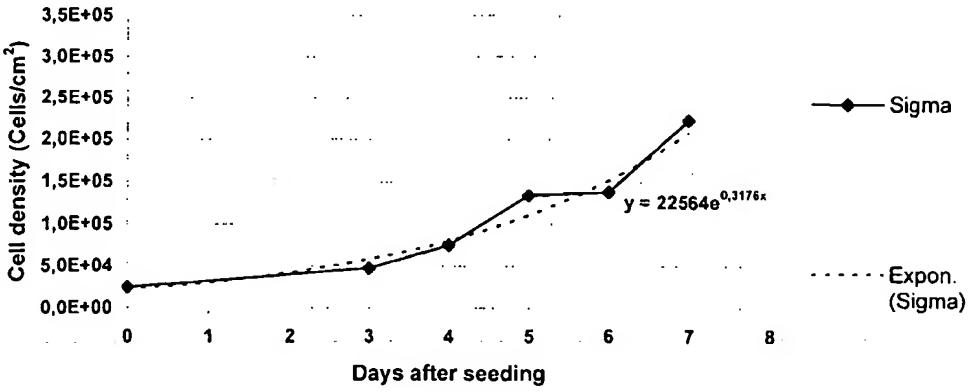


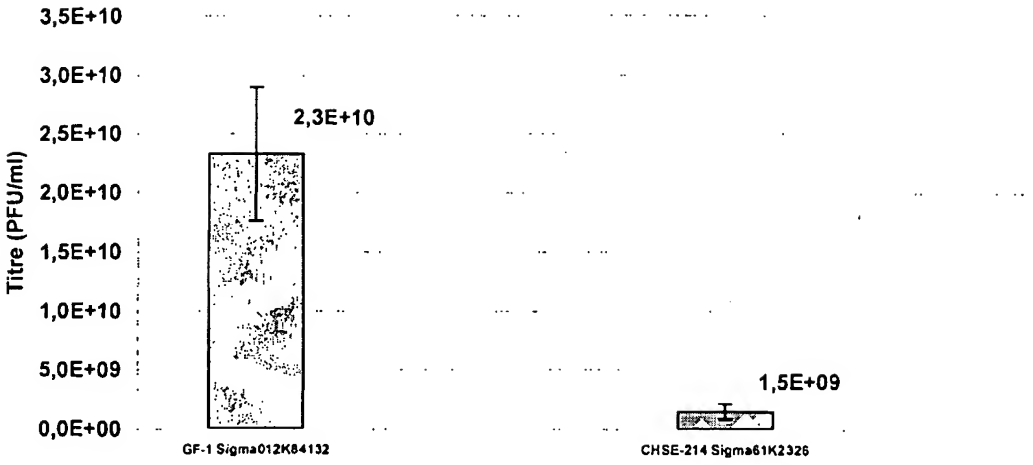

**Figure 2.** Cell growth promotion test on GF-1 cells with 75 $cm^2$ cell culture flasks. Two flasks were counted at each time point.




*(B) Test for IPNV yields*

The average IPNV titre for the CHSE-214 cells were 1.5 x $10^9$ PFU/ml (figure 3). The average IPNV titre for the GF-1 cells grown with serum were 2.3 x $10^{10}$ PFU/ml (figure 3).

**Figure 3.** Average IPNV titres in supernatants from GF-1 and CHSE-214 cell cultures and infected with IPNV.






5. It is my understanding, based on my knowledge and experience in the field of marine fish diseases, that grouper is not a susceptible host for IPNV so that IPNV would not propagate in grouper. On the other hand, it is well-known in the field that salmon is susceptible to IPNV. In fact, it has been found that IPNV caused major outbreak in salmonid species, including trout and salmon. Thus, I was astonished, based on the results of my comparative studies of IPNV titers in the GF-1 and CHSE-214 cell lines, that IPNV is actually propagated in a grouper cell line. I was even more surprised to find out that the titer of IPNV in the GF-1 cell line was more than 10 times higher that that in the CHSE-214 cell line, as salmon is known to be susceptible to IPNV and grouper is not.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the

like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

31 August 2005 — Date

Kjersti Gravingen — Kjersti Gravingen